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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,246	04/07/2006	John Jairo Lopez Areiza	270932US0PCT	1301
22850 7590 09/19/2007 OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			EXAMINER RUSSEL, JEFFREY E	
			ART UNIT 1654	PAPER NUMBER
			NOTIFICATION DATE 09/19/2007	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary

Application No.

10/537,246

Applicant(s)

LOPEZ AREIZA ET AL.

Examiner

Jeffrey E. Russel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 April 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 and 20-27 is/are rejected.
- 7) ☒ Claim(s) 13-19 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>20050601</u> . | 6) <input type="checkbox"/> Other: _____ |

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1. The Sequence Listing filed April 7, 2006 has been approved.
2. The disclosure is objected to because of the following informalities: “(SEQ ID NO:1)” should be inserted after each of the amino acid sequences recited at page 3, line 13. See 37 CFR 1.821(d). Appropriate correction is required.
3. Claims 20-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 20 and 21 are indefinite because they are incomplete. Claims 20 and 21 recite compounds of Formulae I, III, IV, V, and VI, but these formulae are not recited in the claims. Where possible, claims are to be complete of themselves. See MPEP 2173.05(s).
4. Claims 7 and 13-20 are objected to because of the following informalities: At claim 7, line 3, “NH2” should be changed to “NH₂”. “SEQ ID NO:1” should be inserted after each of the amino acid sequences recited in claim 7. See 37 CFR 1.821(d). At claim 13, line 3, “an” should be deleted. At claim 13, line 5, “a” should be changed to “an”. Appropriate correction is required.
5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. *Joy Technologies Inc. v. Quigg*, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. *In re Hoeschele*, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. *In re Clinton*, 188 USPQ 365, 367 (CCPA 1976); *In re Thompson*, 192 USPQ 275, 277 (CCPA 1976).

6. Claims 1-12 and 23-27 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 01/34631 in view of the Gante article (Synthesis, No. 6, pages 405-413) or the WO Patent Application 97/35199. The WO Patent Application '631 teach inhibitory peptides capable of inhibiting β pleated sheet formation in amyloid β peptide. The base peptide/lead compound to be modified is LPFFD, and modifications include N-terminal acetylation and C-terminal amidation, and modification of the α -carbon atoms. Because of the inhibitory activity, the peptides are useful in preventing or treating Alzheimer's disease. The peptides are combined with pharmaceutically acceptable carriers and excipients for administration. See, e.g., page 8, lines 4-9; page 10, lines 16-21; page 12, line 12; page 12, line 19 - page 13, line 5; page 23, line 9 - page 24, line 7; page 25, line 10 - page 26, line 21; and claims 1-6 and 17. The WO Patent Application '631 does not teach a peptide in which one or more of the α -carbon atoms is replaced with a nitrogen atom, i.e. in which aza-amino acids are used, and does not teach a peptide using aza-amino acids, N-terminal acetylation, and C-terminal amidation. The Gante article teaches azapeptides, in which an α -carbon atom is replaced with a nitrogen atom. The azapeptides are easy to synthesize, and can result in a peptide having a

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longer duration of action and sometimes increased activity with respect to the peptide that was modified. See, e.g., page 405, paragraph bridging columns 1 and 2, and section 5. The WO Patent Application '199 teaches a wide variety of azapeptides with therapeutic activity. The azapeptides have the benefit of easy synthesis, resistance to enzymatic cleavage, and sometimes greater activity than the parent peptides. See page 2, line 35 - page 4, line 30. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to modify the LPFFD lead compound of the WO Patent Application '631 by introducing azaamino acids at any or all locations in the peptide, because the WO Patent Application '631 teaches LPFFD to be a lead compound for the design of therapeutic agents for preventing or treating Alzheimer's disease, and because the Gante article and the WO Patent Application '199 teach that azapeptides are known to be useful for the synthesis of peptidomimetics which have the benefit of increased stability and sometimes greater activity with respect to the base peptide. It would further have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to also modify such azapeptides of the WO Patent Application '631 in view of the Gante article and the WO Patent Application '199 by also acetylating the N-terminus and amidating the C-terminus of the azapeptides, because the WO Patent Application '631 teaches that such modifications protect against digestion by aminopeptidase and carboxypeptidases, and teaches that multiple modifications can be made to the lead compound in order to protect against proteolysis. See, e.g., page 12, line 19 - page 13, line 5, and page 18, lines 18-22. It is prima facie obvious to apply the known techniques of peptide stabilization, i.e. of amidating and acetylating peptides and forming peptidomimetics, to the lead compound of the WO Patent Application '631, because these techniques are recognized as part of the ordinary capabilities of

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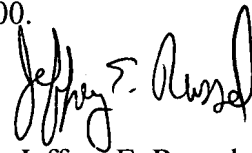
one of ordinary skill in the art and would have been expected to yield the predictable result of increasing the resistance to enzymatic cleavage of the lead compound (see the WO Patent Application '631, the Gante article, and the WO Patent Application 631).

7. Claims 13-19 would be allowable if rewritten or amended to overcome the claim objections set forth in this Office action. Claims 20-22 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, and the claim objections set forth in this Office action. The prior art of record does not teach or render obvious the method steps of instant claim 13 in which a compound of Formula (II) is subjected to the recited reacting and removing steps. While Monguzzi et al (U.S. Patent No. 4,178,444) at column 5, lines 60-61, teach a compound meeting the requirements of Formula (II) (in which R and A are both H), the compound of Monguzzi et al is not subjected to any process similar or analogous to that recited in Applicants' claims. With respect to instant claims 21 and 22, the prior art of record does not teach or render obvious compounds having the recited structures. The German Patent 2,246,282 (see in particular the compound at page 15, third entry from the bottom of the table) is the closest in structure to Applicants' compound of formula (III). However, the compound of the prior art lacks a methylene group between the phenyl ring and the hydrazine group. The prior art of record does not provide any suggestion or any other rationale which would render the insertion of a methylene group into the compound of the German Patent '282 prima facie obvious, especially in view of the disparate uses of the prior art's and Applicants' compounds.

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8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel

Primary Patent Examiner

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JRussel

September 10, 2007